REMARKS

Applicant requests reconsideration of the application in view of the discussion that follows. The status of the claims as of this response is as follows: Claims 1-6, 13-25, 27, 30 and 31 are pending. Claims 1-12, 14, 20, 22, 23, 26, 28, 29 and 32 were previously canceled. No claims were amended herein.

Rejection under 35 U.S.C. §103

Claims 13, 15-19, 21, 24, 25, 27, 30 and 31 were rejected again under 35 U.S.C. §103(a) as unpatentable over Hui, *et al.* (EP 1,340,981 A2) (Hui) in view of Avenia, *et al.* (U.S. Patent No. 4,041,076) (Avenia).

The Office Action asserts that Hui discloses various competitive and noncompetitive methods/assays and a kit for detection and quantitative determination of amphetamine derivatives such as MDA, MDMA, MDEA, MDPA, BDB, and MBDB using antibody against amphetamine derivatives and label derivatives (such as fluorescent, luminescent, radioactive isotope, etc.). Hui's amphetamine derivatives and immunogens, continues the Office Action, are similar to the compound and immunogen of the present invention and are expected to recognize different amphetamine derivatives suitable for different immunoassays. However, recognizes the Office Action, the linking group or the position of linker at the amphetamine derivative is different from the present compound. The Office Action asserts further that Avenia discloses an amphetamine immunogen, labeled tracer and antibodies and discloses a competitive immunoassay method for detection of phenethylamines (e.g. norepinephrine, dopamine, epinephrine and amphetamines). The immunogen of Avenia, contends the Office Action, is the same as the immunogen of the present application. The Office Action further asserts that, since detection of amphetamine, methamphetamine and their derivatives is important in the field of ecstasy drug and once a hapten, immunogen or an antibody is available, one would obviously try to use the hapten and the immunogen in different immunoassay methods to develop a better detection assay for the drug. The Office Action concludes that it would have been obvious at the time of the invention to a person of ordinary skill in the art to substitute equivalent hapten, immunogen or antibody as disclosed by Avenia in the method of Hui with the expectation of obtaining a

similarly useful immunoassay method and kit for detection of amphetamine and amphetamine derivatives.

Claim 13 is directed to a method for determining a compound selected from the group consisting of 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxy-methamphetamine (MDMA), 3,4-methylenedioxyethylamphetamine (MDEA) and 4-hydroxy-3-methoxy-methamphetamine (HMMA). A sample suspected of containing the compound is combined with an antibody raised against the compound as designated in claim 13 and with a label conjugate of the formula set forth in the claim. Neither Hui nor Avenia disclose or suggest such a label conjugate. The disclosure of Avenia is directed to immunogens for preparing antibodies specific for certain amphetamine derivatives. To that end, Avenia prepares antigens by covalently linking a hapten of the formula indicated in the reference to a conventional immunogenic carrier. The patentee indicates that suitable proteins may be employed as the conventional immunogenic carrier such as gamma globulins and serum albumins of human and other animal origins.

There is no mention in Avenia of conjugates of labels and the haptens of the reference. There is no mention of conjugates of enzymes and the haptens of the reference. This is consistent with the teaching of Avenia, who is concerned with conventional immunogenic carrier conjugates and not with label conjugates. The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. Furthermore, Avenia goes on to state that his assays using the above reagents were superior in all cases to assays utilizing free radical labels and enzyme labels. Accordingly, Avenia does not disclose or suggest the label conjugates of claim 13, and, furthermore, it may be argued that Avenia teaches away from such conjugates. Therefore, the motivation for the skilled artisan to combine the teachings of Hui and Avenia is not sufficient.

The Office Action responded to the above argument by asserting that Avenia clearly envisaged using labeled phenethylamine in a competitive immunoassay using antibody against phenethylamine conjugate (referring to Avenia, column 4, lines 35-58). It is clear from the cited paragraph that the reference is discussing labeled

phenethylamine and not labeled haptens of the disclosure of Avenia. The reference does not disclose or suggest using the disclosed haptens conjugated to a label. The only conjugates of the haptens of the reference are those of the haptens with immunogenic carriers. This lack of disclosure or suggestion in the reference, when combined with Avenia's teaching that his assays using his reagents including a radiolabeled phenethylamine were superior in all cases to assays utilizing free radical labels and enzyme labels, must negative any motivation that one skilled in the art might have to make the substitution as argued in the Office Action. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills,* 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)

Furthermore, the Office Action at the top of page 5 argues that one would obviously try to use the hapten and the immunogen in different immunoassay methods. However, obvious to try is not the standard.

The Federal Circuit has held that the mere fact that the prior art may be modified in the manner suggested by an examiner does not make the modification obvious unless the prior art suggested the desirability of the modification (*In re Fine*, 837 F. 2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988)). In the present situation there is no teaching or suggestion in Avenia to use label conjugates of his haptens in an assay method. It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Fritch*, 972 F. 2d 1260, 23 USPQ 2d 1780 (Fed. Cir. 1992), quoting *In re Fine*, *supra*.

Furthermore, according to M.P.E.P. 2143.03, all claim limitations must be taught or suggested by the prior art in order to establish *prima facie* obviousness (citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). In the present situation, the combined teachings of the references do not disclose or suggest the presently claimed label conjugates.

Claims 15-18 depend ultimately from claim 13 and are, therefore, patentable over

the combination of the teachings of Hui and Avenia by virtue of such dependency since claim 13 is patentable over Hui and Avenia as demonstrated above. If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) (M.P.E.P. 2143.03).

Claim 19 is patentable over the combined teachings of the references because Avenia and Hui do not disclose or suggest label conjugates as claimed. As mentioned above, Avenia arguably teaches away from labels other than radioactive labels and, furthermore, does not disclose or suggest radioactive label conjugates of the formula claimed in claim 19. Therefore, as mentioned above, the motivation for the skilled artisan to combine the teachings of Hui and Avenia is not sufficient.

Claims 21, 24 and 25 are patentable over the combined teachings of Hui and Avenia for reasons similar to those presented above with respect to the rejection of claim 13 over Hui and Avenia. There is no mention in Avenia of conjugates of labels, including enzyme labels, and the haptens of the reference. This is consistent with the teaching of Avenia, who is concerned with conventional immunogenic carrier conjugates. The labeled derivative that Avenia employs in his assay is a radioactive amphetamine analog prepared by iodination with radioactive iodine of racemic 4-hydroxy-alpha-methylphenethylamine hydrobromide. Furthermore, Avenia goes on to state that his assays using the above reagents were superior in all cases to assays utilizing free radical labels and enzyme labels. Accordingly, Avenia does not disclose or suggest the label conjugates of claim 13 and the reference, it may be argued, teaches away from such conjugates. The motivation for the skilled artisan to combine the teachings of Hui and Avenia is not sufficient.

Claim 27 is directed to a method for determining methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine in a sample suspected of containing methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine. A sample is combined in a medium with a conjugate of an enzyme and a methylenedioxyamphetamine analog and a conjugate of an enzyme and a methylenedioxymethamphetamine analog and a conjugate of an enzyme and a methylenedioxyethamphetamine analog, and with an

antibody for methylenedioxyamphetamine raised against a compound of the formula as claimed, and an antibody for methylenedioxymethamphetamine raised against a compound of the formula as claimed, and an antibody for methylenedioxy-ethamphetamine raised against a compound of the formula as claimed. The medium is examined for the presence of a complex comprising the methylenedioxyamphetamine and the antibody for methylenedioxyamphetamine and a complex of the methylenedioxymethamphetamine and the antibody for methylenedioxy-methamphetamine and a complex of the methylenedioxyethamphetamine and the antibody for methylenedioxyethamphetamine, the presence thereof indicating the presence of the methylenedioxyamphetamine and/or methylenedioxymethamphetamine and/or methylenedioxyethamphetamine in the sample.

The combination of Hui and Avenia does not disclose or suggest the method of claim 27 where the sample is combined with all three antibodies as claimed. Furthermore, as discussed above, there is no mention in Avenia of conjugates of labels, including enzyme labels, and the haptens of the reference. As discussed above, there is a lack of motivation for the skilled artisan to combine the teachings of Hui and Avenia in the manner in which the Office Action has done.

For reasons similar to those discussed above, the combined teachings of Hui and Avenia do not disclose or suggest the kits of claims 30 and 31.

Claims 13-25, 27 and 30-31 were rejected under 35 U.S.C. §103(a) as unpatentable over Rouhani, *et al.* (GB 2361473 A) (Rouhani) in view of Avenia.

Without acquiescing in the arguments in the Office Action, Applicant submits that the cancellation of claims 14, 20, 22 and 23 above renders this ground of rejection moot with regard to those claims.

Furthermore, Applicant submits that claims 13, 15-19, 21, 24, 25, 27 and 30-31 are patentable over the combined teachings of Rouhani and Avenia for reasons similar to those set forth above with respect to the rejection of the above claims over the combined teachings of Hui and Avenia.

Conclusion

Applicant has demonstrated that Claims 13, 15-19, 21, 24, 25, 27, 30 and 31 satisfy the requirements of 35 U.S.C. §103. Allowance of the above-identified patent application, it is submitted, is in order.

Respectfully submitted,

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